R E M A R K S

Telephone Interviews With the Examiner

December 1, 2009 Telephone Interview

The undersigned had a telephone interview with Examiner Sznaidman on December 1, 2009. The report of such interview is as follows.

Examiner Sznaidman suggested that the independent claims be limited to the range of concentration of the compound set forth in Table 6 on page 20 of the specification. Examiner Sznaidman said that it is not, however, a certainty that claims limited in this matter would be allowed. The undersigned then proposed that instead of limiting the claims to a range of concentration of the compound, that the independent claims be amended to include "functional language" (such as reciting an amount of the compound effective for inhibiting mycotoxin production produced by a plant pathogenic fungi of a cereal in the absence of controlling the degree of proliferation of the plant pathogenic fungi). Examiner Sznaidman said, however, that the recitation of such "functional language" in the independent claims may not be sufficient to overcome the prior art rejection

During said December 1, 2009 telephone interview, Examiner Sznaidman raised the following questions, which are addressed

hereinbelow:

1. How is mycotoxin production inhibited in both the presence and absence of the degree of Fusarium head blight ("FHB") (see page 21, lines 15 to 21 of the present specification)?

2. Examiner Sznaidman said that it appeared from Table 6 on page 20 of the specification that the amount of Fusarium head blight fungus is almost constant at concentrations of potassium phosphite from 0.056% to 0.56%, yet in an amount of only 0.41 ppm, or less than the detection limit. How or why does this occur?

3. Examiner Sznaidman asked for an explanation why the results set forth in said Table 6 are "unexpected."

4. What is the advantage of reducing mycotoxin when the fungi are at an almost constant amount in said Table 6?

No agreement was reached during the December 1, 2009 telephone interview.

The following are applicants' responses to the aforesaid questions raised by Examiner Sznaidman during the December 1, 2009 telephone interview.

1. Mycotoxin is a metabolite of some kinds of fungi. Some kinds of fungi cause Fursarium head blight infection and proliferation in a plant. During the proliferation, some kinds of fungi produce mycotoxin as its metabolite and secrete it from their bodies. The

present inventors consider that the compounds recited in applicants' present claims, such as potassium phosphite, attack a part of the metabolic pathway of mycotoxin production and inhibit production of mycotoxin from fungi. This inhibition may not be strong enough to kill fungi or to suppress FHB appearance in an infected plant. No. 4 in Table 1 on page 10 of the present specification shows that when a compound recited in applicants' present claims is applied, mycotoxin production was inhibited in a low concentration, even though FHB was not sufficiently suppressed.

2. The answer to the aforesaid question 2 is almost the same as the answer to the above question 1. The present inventors consider that the mechanism of mycotoxin production inhibition by the compounds of the presently claimed invention are different from that of the fungicidal action of conventional fungicides. As shown in Table 6 on page 20 of the present specification, the amount of Fusarium head blight fungi remains almost at a constant level, regardless of the potassium phosphite concentration from 0.056% to 0.56%. On the other hand, mycotoxin concentration is inhibited from ND to 1.60 ppm, depending on the dose applied. This means that it is not necessary to kill all fungus to reduce the mycotoxin level when a compound of the presently claimed invention is applied. This is the key of the presently claimed invention. The compounds recited in

applicants' claims have a very specific feature that the effective dose of mycotoxin production inhibition is different and much lower than that of an amount to reduce fungi.

3. A person of ordinary skill in the art would expect that when mycotoxin producing fungi remains in a plant, mycotoxin will be produced and detected at a certain level, depending on the amount of existing fungi. This recognition is confirmed from the control data shown in Table 5 on page 19 of the present specification, wherein mycotoxin concentration increases depending on the amount of fungi existing in wheat in the non-treatment columns.

As stated above in the answer to question 1, it is known that mycotoxin is a kind of metabolite of fungi. Therefore, a person of ordinary skill in the art would expect that as long as fungi exists in a plant, mycotoxin will be produced from the fungi. Prior to the present invention, when it was attempted to reduce mycotoxin contamination lower than the desired level, it was considered to kill all the fungi in the plant, since the FDA regulation of mycotoxin concentration in cereal is very strict, and as low as less than 1 ppm.

Please refer to the Title and Abstract of Pirgozliev et al. The purpose of Pirgozliev et al. was to control the mycotoxin level in wheat grain in a low level by applying fungicides, but they could

not reach a sufficient result. When fungi remains, mycotoxin will be detected. Taking an opposite viewpoint, when mycotoxin is detected, fungi may remain and need to be killed by increasing the dose of fungicide. This would have been the normal recognition of the ordinary worker in this field at a time prior to the present invention.

The present invention relies on an unexpected result that even if there exists fungi in a cereal such as wheat, mycotoxin concentration is inhibited to a low enough level by applying the compounds as recited in applicants' claims as shown in Table 6 on page 20 of the specification.

4. It is regulated by the FDA to control mycotoxin concentration in cereals to a specific low level, because it is well known that when mycotoxin contaminated cereal was ingested by human beings or by farm animals, it causes health hazards. Therefore, to reduce mycotoxin in cereals would satisfy a long felt need. It had previously been believed that the most effective method was to treat plants with fungicides. In fact, fungicide treatment had been carried out expecting not only to suppress disease, but also to obtain mycotoxin free cereal. But it had been reported very often that treating plants only with a conventional fungicide was not sufficient to avoid mycotoxin contamination in cereals. Once mycotoxin is detected in cereals, they lose economic value in the marketplace.

Heretofore very severe problems occurred, such as in the case shown in No. 7 of Table 2 on page 12 of the specification. The wheat was treated with a conventional control (method) and harvested as healthy grain from their appearance, but they were still contaminated with mycotoxin. Since mycotoxin contamination cannot be noticed from their appearance, it may cause health hazards to the consumer when this contaminated grain is distributed to the marketplace without analysis of mycotoxin concentration. To avoid this problem, there needed to be established a mycotoxin detecting system before the grain is delivered to the marketplace.

The compounds recited in applicants' present claims are very beneficial from this point of view. If one uses the presently claimed invention, he or she can obtain healthy cereal, i.e., mycotoxin free cereal. When the compounds recited in applicants' present claims are applied to a plant, no mycotoxin will remain in the cereal, and the effective dose of inhibition of mycotoxin is lower than the amount for reducing fungi in plant. This is a big advantage compared to the use of conventional fungicides from the viewpoint of safety.

The inhibition of mycotoxin contamination in cereal can provide a widespread profit in a wide ranging area, like the safety of food, avoidance of a health hazard, avoidance of increasing cost in distribution and so on. Therefore, prior to the present invention,

there was a need to introduce a new effective method to avoid mycotoxin contamination in grain other than the insufficient conventional fungicide treatment.

December 15, 2009 Telephone Interview

The undersigned had a telephone interview with Examiner Sznaidman on December 15, 2009. The report of such telephone interview follows.

On December 14, 2009, the undersigned facsimile transmitted to Examiner Sznaidman a proposed amendment to claim 11 for the purpose of having a telephone interview. The gist of said proposed amendment is as follows:

"A method for reducing mycotoxin contamination in a cereal comprising a step of applying ~~to the cereal an amount of~~ at least one compound ~~effective for inhibiting production of mycotoxin by plant pathogenic fungi of cereals~~ selected from the group ...combinations thereof to a plant of a cereal in an amount sufficient for inhibiting mycotoxin production from plant pathogenic fungi in the cereal."

During the December 15, 2009 telephone interview with Examiner Sznaidman, the Examiner said that such proposed amendment would not overcome the current prior art rejection.

The undersigned then discussed with Examiner Sznaidman an alternate claim amendment involving adding the following terminology to the end of claim 11: "in an amount sufficient for inhibiting mycotoxin production from plant pathogenic fungi in a cereal without suppressing said fungi proliferation in a plant." Examiner Sznaidman said that this proposed amendment was an improvement over the proposed amendment facsimile transmitted to him on December 14, 2009, but that this proposed amendment was not sufficient to overcome the current prior art rejection.

The undersigned then raised the possibility of amending claim 11 in the manner that claim 11 is amended in the above "listing of claims." Examiner Sznaidman said that this would be the best option to overcome the current prior art rejection. Examiner Sznaidman said that he could not be certain that such amendment to claim 11 would result in an allowance. Examiner Sznaidman said that if the independent claims were amended to include the limitation discussed hereinabove (i.e., the limitation included in amended claim 11 in the above "listing of claims"), that he would reconsider the current prior art rejection in view of this limitation and, if necessary, conduct a further search for additional prior art.

Claim Amendments

The amendment to claims 1 and 31 concerning "a plant of a cereal" is supported in the specification on page 8, line 11; page 13, line 16; and page 16, line 7.

The amendment to claims 1 and 31 of "up to an amount of 0.56 wt% as converted to P_2O_5" is supported in the specification in Table 6 on page 20.

Applicants have informed the undersigned that in the aforesaid terminology of "0.56 wt%," the term "wt%" refers to W/V (kg/L) as in the concentration of the effective ingredient of fungicides shown in Table 3 in the specification, etc. In Example 1 of the specification, it is described that the respective fungicides are diluted (several thousandths time dilution) and the fungicides are sprayed with a predetermined volume per area (100 L per 10 a) (see page 8, line 10 of the specification). In this art, the expression "wt%" thus means "W/V (kg/L)."

Claim 16 was amended to depend on claim 11.

The amendment to claim 20 involves reciting a claim dependency (claim 16) that was recited in claim 20 prior to the AMENDMENT UNDER 37 CFR 1.111 filed July 15, 2009.

Claim 35 was amended to correct the dependency thereof.

Presently Claimed Invention

The presently claimed invention is directed to a method for reducing mycotoxin contamination based on an inhibitory effect on mycotoxin production from plant pathogenic fungi in a cereal comprising a step of applying at least one compound effective for inhibiting production of mycotoxin by plant pathogenic fungi of cereals, wherein the compound is selected from the group consisting of an ammonium salt, a primary to quaternary ammonium salt, an alkali metal salt, an alkaline earth metal salt and a polyvalent metal salt of phosphorous acid or a phosphite ester to a plant of a cereal in an amount sufficient for inhibiting mycotoxin production from plant pathogenic fungi in a cereal up to an amount of 0.56 wt% as converted into P_2O_5 (see applicants' claim 11).

The presently claimed invention also concerns a method for reducing mycotoxin contamination in a cereal comprising a step of applying to a plant of a cereal an amount of potassium phosphite effective for inhibiting production of mycotoxin by plant pathogenic fungi of cereals in a cereal up to an amount of 0.56 wt% as converted into P_2O_5 (see applicants' claim 31).

In applicants' dependent claims 30, 32 and 35, the mycotoxin is specified to be deoxynivalenol ("DON").

Applicants' dependent claim 35 recites that the cereal is wheat; the mycotoxin is deoxynivalenol; the deoxynivalenol is reduced to 1.1 ppm or less; and the compound is potassium phosphite.

The gist of the presently claimed invention is inhibition of a mycotoxin, such as DON, not based on a fungicidal effect of phosphite compounds, and not based on blocking production of mycotoxin by killing mycotoxin-producing fungi. Rather, the present inventors were the first to discover that the compounds recited in applicants' claims have the effect of reducing an amount (a producing amount) of a mycotoxin, such as DON, produced in a cereal, even when *Fusarium* head blight ("FHB") (a crop disease) is generated in a plant body or even when *Fusarium* fungi remains the same.

It is clear that a mycotoxin, such as DON, will not be produced when the fungi causing the mycotoxin does not exist, such as the suppression of the fungi by a fungicide. It is also evident that when a phosphite compound such as potassium phosphite is administered within a certain concentration, a certain fungicidal effect may be obtained. However, the presently claimed invention is directed to inhibiting the effect of a mycotoxin, such as DON, by applying a compound, such as a phosphite compound, without necessarily bringing about a fungicidal effect.

Obviousness Rejection Under 35 USC 103

Claims 11 to 13, 15 to 18, 20 to 25, 27 to 29, 31 to 34 and 35 were rejected under 35 USC 103 as being unpatentable over Staub et al. (USP 4,849,219) in view of Pirgozliev et al. (European Jour. of Plant Pathology (2002) 108:469-478) for the reasons set forth beginning at the middle of page 3 and continuing to the bottom of page 7 of the September 15, 2009 Office Action.

It was admitted in the previous Office Action of April 17, 2009 that Staub et al. do not teach reducing mycotoxin, wherein the mycotoxin is deoxynivalenol. More to the point, Staub et al. do not mention any mycotoxin.

Staub et al. concern microbicides. Staub et al. is directed to a fungicidal composition. In the paragraph bridging columns 3 and 4, Staub et al. describe over twenty-five different fungicides. In column 5, Staub et al. list almost seventy different species of plants and fifteen different fungi.

In contrast to Staub et al., the purpose of the presently claimed invention is to inhibit the production of a mycotoxin by a compound as recited in applicants' claims, even if *Fusarium* head blight exists in a plant. There is no specific reason to select a compound as recited in applicants' claims, such as potassium phosphite, from the fungicides disclosed in Staub et al. to inhibit mycotoxin

contamination in crops.

Pirgozliev et al. concern only a study wherein metconazole and azoystrobin, fungicides used for the control of Fusarium head blight, resulted in elevated concentration of deoxynivalenol mycotoxin.

Pirgozliev et al. do not teach or suggest any of the compounds effective for inhibiting production of a mycotoxin by plant pathogenic fungi of cereals which are recited in applicants' claims.

Pirgozliev et al. disclose the effects of prevention of FHB and reduction of the concentration of a mycotoxin by specific chemicals, such as azoxystrobin or metconazole. But there is no description or suggestion for prevention of FHB or inhibiting a mycotoxin by a compound as recited in applicants' present claims.

In Staub et al. and Pirgozliev et al., there is no teaching or suggestion concerning the effect of compounds as recited in applicants' claims, such as potassium phosphite, to prevent mycotoxin production.

Accordingly, there would be no reason for a person of ordinary skill in the art to select a compound as recited in applicants' claims to inhibit mycotoxin production based on the disclosures of Staub et al. and Pirgozliev et al.

As disclosed at the middle of page 4 of applicants' specification, it has been demonstrated that not all of the pathogenic

fungi which cause *Fusarium* head blight produce DON contamination.

Accordingly, based on the knowledge involving *Fusarium* head blight, it is respectfully submitted that one of ordinary skill in the art would not know precisely what fungicide to apply to reduce a mycotoxin, such as DON, to an acceptable safe level.

The presently claimed invention selectively reduces a mycotoxin to a level approved by the FDA, regardless of the presence or absence or the degree of *Fusarium* head blight of cereals.

As discussed in the paragraph bridging pages 4 and 5 of the present specification, even when the *Fusarium* head blight of the cereals is controlled by combined application of various fungicidal agents, DON is frequently detected at more than 1.1 ppm.

In view of the above, it is respectfully submitted that one of ordinary skill in the art would not consider combining Staub et al. and Pirgozliev et al. to arrive at applicants' presently claimed invention. Even assuming *arguendo* that the references were combinable, it is respectfully submitted that such combination would not lead one of ordinary skill in the art to the presently claimed invention.

The following position was taken at the top of page 5 of the September 15, 2009 Office Action:

> "Pirgozliev et al. teach that the FDA recommends that DON concentration should not exceed 1000 micrograms/kg (i.e., ppm) in finished wheat product..., the skilled artisan would have been further motivated to determine the amount of potassium phosphite required in order to reduce the amount of DON below the level required by the FDA."

However, the skilled artisan would consider to use an increased amount of the fungicide to such an extent that the respective fungi would not generate FHB as Pirgozliev et al. stated in their Abstract at lines 2 to 4 from the bottom as follows:

> "It is concluded that fungicides, applied for the control of FHB, affect DON concentration indirectly by influencing the amount of trichlothecene-producing *Fusarium* species present in wheat grain."

The characteristic feature of the presently claimed invention resides in applying a compound as recited in applicants' claims that does not necessarily completely kill the fungi, but prevent mycotoxin production. Such result is submitted to be remarkably surprising and indeed could not be expected from using conventional fungicides.

In reply to the "Examiner's response" beginning on line 8 on page 6 of the September 15, 2009 Office Action, it is noted that on page 4, lines 14 to 24 of the present specification, it is disclosed that there exists several kinds of FHB fungi, some of them produce

a mycotoxin and others do not, and fungicides effective to eradicate or reduce these fungi are different from each other. Thus, disease protection afforded by applying fungicidal agents do not sufficiently prevent DON contamination in all cases (see page 4, lines 28 to 30 of the present specification).

Also, in the Tables in the present specification, it has been shown that in some cases, even when a fungicide prevents FHB, DON contamination exceeded the level (1.1 ppm) approved by the FDA (see Table 1 on page 10 of the present specification, Sample Nos. 1, 6 and 7). Even in the case where mycotoxin contamination could not be prevented only by a conventional fungicide, it can be prevented by applying a compound as recited in applicants' claims.

In reply to the "Examiner's response" beginning on page 6, line 14 and continuing to the bottom of page 7 of the September 15, 2009 Office Action, it is noted that if the DON producing fungi could be suppressed completely, DON contamination can certainly be avoided. This is the same idea as attempting to prevent DON by using a conventional fungicide. It appears that the Examiner considers that the compounds recited in applicants' claims are the same as conventional fungicides. However, as stated on page 7, lines 1 to 7 of the September 15, 2009 Office Action, the preventing of DON production by applying the compounds recited in applicants' claims

is not the same as the eradication or reduction of the fungi.

In the presently claimed invention, it is not necessarily required to completely kill the fungi in order to prevent the production of a mycotoxin. As pointed out by the Examiner and as discussed in the present specification, the growth of the fungi may be affected by an amount of a phosphite compound. However, this fungicidal function of a phosphite compound is a subsidiary effect. As acknowledged on page 7, lines 5 to 7 of the September 15, 2009 Office Action, the prevention of mycotoxin production afforded by the presently claimed invention is based on a quite different and novel mechanism from a fungicidal effect. Such an effect is not found in any of the prior art references, and the effect was first discovered by the present inventors.

Withdrawal of the 35 USC 103 rejection is therefore respectfully requested.

Additional Considerations

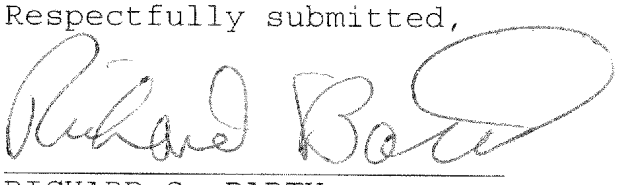
As discussed above, the presently claimed invention satisfies a long felt need in the art.

Applicants have informed the undersigned that corresponding applications in Europe, Australia and New Zealand have been allowed.

Reconsideration is requested. Allowance is solicited.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

Respectfully submitted,



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